

# PATENT COOPERATION TREATY

**PCT**

## NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

TETAZ, Franck  
Rhône-Poulenc Agro  
14/20, rue Pierre Balzet  
F-69009 Lyon  
FRANCE

<b>Date of mailing (day/month/year)</b> 14 March 2000 (14.03.00)	
<b>Applicant's or agent's file reference</b> PH 97069	<b>IMPORTANT NOTIFICATION</b>
<b>International application No.</b> PCT/EP98/06977	<b>International filing date (day/month/year)</b> 09 October 1998 (09.10.98)

**1. The following indications appeared on record concerning:**

☐ the applicant
 ☐ the inventor
 ☒ the agent
 ☐ the common representative

<b>Name and Address</b> TETAZ, Franck Rhône-Poulenc Agro 14/20, rue Pierre Balzet F-69009 Lyon France	<b>State of Nationality</b>	<b>State of Residence</b>
	<b>Telephone No.</b> (33) 4 72 85 25 92	
	<b>Facsimile No.</b> (33) 4 72 85 28 43	
	<b>Teleprinter No.</b>	

**2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:**

☐ the person
 ☐ the name
 ☒ the address
 ☐ the nationality
 ☐ the residence

<b>Name and Address</b> TETAZ, Franck Aventis Cropscience S.A. 55, avenue René-Cassin F-69009 Lyon France	<b>State of Nationality</b>	<b>State of Residence</b>
	<b>Telephone No.</b> (33) 4 72 85 26 36	
	<b>Facsimile No.</b> (33) 4 72 85 28 43	
	<b>Teleprinter No.</b>	

**3. Further observations, if necessary:**

**4. A copy of this notification has been sent to:**

<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned
<input checked="" type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No.: (41-22) 740.14.35	<b>Authorized officer</b>  R. Chrem  Telephone No.: (41-22) 338.83.38
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## PATENT COOPERATION TREATY

PCT

From the INTERNATIONAL BUREAU

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

To:

TETAZ, Franck  
Rhône-Poulenc Agro  
14/20, rue Pierre Baizet  
F-69009 Lyon  
FRANCE

Date of mailing (day/month/year) 14 March 2000 (14.03.00)	<b>IMPORTANT NOTIFICATION</b>
Applicant's or agent's file reference PH 97069	
International application No. PCT/EP98/06977	International filing date (day/month/year) 09 October 1998 (09.10.98)

1. The following indications appeared on record concerning:		
<input checked="" type="checkbox"/> the applicant	<input type="checkbox"/> the inventor	<input type="checkbox"/> the agent <input type="checkbox"/> the common representative
Name and Address RHONE-POULENC AGRO 14/20, rue Pierre Baizet F-69009 Lyon France	State of Nationality FR	State of Residence FR
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:		
<input type="checkbox"/> the person	<input checked="" type="checkbox"/> the name	<input checked="" type="checkbox"/> the address <input type="checkbox"/> the nationality <input type="checkbox"/> the residence
Name and Address AVENTIS CROPS SCIENCE S.A. 55, avenue René Cassin F-69009 Lyon France	State of Nationality FR	State of Residence FR
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
3. Further observations, if necessary:		
4. A copy of this notification has been sent to:		
<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned	
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned	
<input checked="" type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:	

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer  R. Chrem
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark  
Office  
(Box PCT)  
Crystal Plaza 2  
Washington, DC 20231  
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 07 June 1999 (07.06.99)	
International application No. PCT/EP98/06977	Applicant's or agent's file reference PH 97069
International filing date (day/month/year) 09 October 1998 (09.10.98)	Priority date (day/month/year) 10 October 1997 (10.10.97)
Applicant DOUTRIAUX, Marie-Pascale et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

03 May 1999 (03.05.99)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer A. Karkachi Telephone No.: (41-22) 338.83.38
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# PCT

## REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For receiving Office use only

**PCT/EP 98 / 06 977**

International Application No.

**09 OCT 1998**

**(09. 10. 1998)**

International Filing Date

**EUROPEAN PATENT OFFICE  
PCT INTERNATIONAL APPLICATION**

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference  
(if desired) (12 characters maximum) **PH 97069**

**Box No. I TITLE OF INVENTION**

**Methods for obtaining plant varieties**

**Box No. II APPLICANT**

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

**RHONE-POULENC AGRO  
14/20 Rue Pierre Baizet  
69009 LYON  
FRANCE**

☐ This person is also inventor.

Telephone No.

**(33) 4 72 85 26 41**

Facsimile No.

**(33) 4 72 85 28 43**

Teleprinter No.

State (that is, country) of nationality:  
**FR**

State (that is, country) of residence:  
**FR**

This person is applicant for the purposes of: ☐ all designated States ☒ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

**Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)**

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

**DOUTRIAUX Marie-Pascale  
64 Route de Villebon  
91160 SAULX LES CHARTREUX  
FRANCE**

This person is:

☐ applicant only

☒ applicant and inventor

☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:  
**FR**

State (that is, country) of residence:  
**FR**

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

☒ Further applicants and/or (further) inventors are indicated on a continuation sheet.

**Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE**

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as:

☒ agent

☐ common representative

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

**GENIN Patrick  
RHONE-POULENC AGRO  
14/20 Rue Pierre Baizet  
DPI  
69009 LYON  
FRANCE**

Telephone No.

**(33) 4 72 85 26 41**

Facsimile No.

**(33) 4 72 85 28 43**

Teleprinter No.

☐ Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Continuation of Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)	
<b>If none of the following sub-boxes is used, this sheet should not be included in the request.</b>	
<p>Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)</p> <p><b>BETZNER Andreas Stefan</b>  <b>40 Dallachy Place</b>  <b>Page</b>  <b>ACT 2614</b>  <b>AUSTRALIA</b></p>	<p>This person is:</p> <p><input type="checkbox"/> applicant only</p> <p><input checked="" type="checkbox"/> applicant and inventor</p> <p><input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below.)</p>
State (that is, country) of nationality: <b>AU</b>	State (that is, country) of residence: <b>AU</b>
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input checked="" type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box	
<p>Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)</p> <p><b>FREYSSINET Georges</b>  <b>21 Rue de Nervieux</b>  <b>69450 ST CYR AU MONT D'OR</b>  <b>FRANCE</b></p>	<p>This person is:</p> <p><input type="checkbox"/> applicant only</p> <p><input checked="" type="checkbox"/> applicant and inventor</p> <p><input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below.)</p>
State (that is, country) of nationality: <b>FR</b>	State (that is, country) of residence: <b>FR</b>
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input checked="" type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box	
<p>Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)</p> <p><b>PEREZ Pascual</b>  <b>17 Chemin de la Pradelle</b>  <b>Varennnes</b>  <b>63450 CHANONAT</b>  <b>FRANCE</b></p>	<p>This person is:</p> <p><input type="checkbox"/> applicant only</p> <p><input checked="" type="checkbox"/> applicant and inventor</p> <p><input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below.)</p>
State (that is, country) of nationality: <b>FR</b>	State (that is, country) of residence: <b>FR</b>
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input checked="" type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box	
<p>Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)</p>	<p>This person is:</p> <p><input type="checkbox"/> applicant only</p> <p><input type="checkbox"/> applicant and inventor</p> <p><input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below.)</p>
State (that is, country) of nationality:	State (that is, country) of residence:
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box	

☐ Further applicants and/or (further) inventors are indicated on another continuation sheet.

## Box No.V DESIGNATION OF STATES

The following designations are hereby made under Rule 4.9(a) (mark the applicable check-boxes; at least one must be marked):

## Regional Patent

- ☒ **AP ARIPO Patent:** GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SZ Swaziland, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- ☒ **EA Eurasian Patent:** AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- ☒ **EP European Patent:** AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- ☒ **OA OAPI Patent:** BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, specify on dotted line) + GU Guinea-Bissau

## National Patent (if other kind of protection or treatment desired, specify on dotted line):

- |  |  |
|--|--|
| <input checked="" type="checkbox"/> AL Albania                               | <input checked="" type="checkbox"/> LS Lesotho                                   |
| <input checked="" type="checkbox"/> AM Armenia                               | <input checked="" type="checkbox"/> LT Lithuania                                 |
| <input checked="" type="checkbox"/> AT Austria                               | <input checked="" type="checkbox"/> LU Luxembourg                                |
| <input checked="" type="checkbox"/> AU Australia                             | <input checked="" type="checkbox"/> LV Latvia                                    |
| <input checked="" type="checkbox"/> AZ Azerbaijan                            | <input checked="" type="checkbox"/> MD Republic of Moldova                       |
| <input checked="" type="checkbox"/> BA Bosnia and Herzegovina                | <input checked="" type="checkbox"/> MG Madagascar                                |
| <input checked="" type="checkbox"/> BB Barbados                              | <input checked="" type="checkbox"/> MK The former Yugoslav Republic of Macedonia |
| <input checked="" type="checkbox"/> BG Bulgaria                              | <input checked="" type="checkbox"/> MN Mongolia                                  |
| <input checked="" type="checkbox"/> BR Brazil                                | <input checked="" type="checkbox"/> MW Malawi                                    |
| <input checked="" type="checkbox"/> BY Belarus                               | <input checked="" type="checkbox"/> MX Mexico                                    |
| <input checked="" type="checkbox"/> CA Canada                                | <input checked="" type="checkbox"/> NO Norway                                    |
| <input checked="" type="checkbox"/> CH and LI Switzerland and Liechtenstein  | <input checked="" type="checkbox"/> NZ New Zealand                               |
| <input checked="" type="checkbox"/> CN China                                 | <input checked="" type="checkbox"/> PL Poland                                    |
| <input checked="" type="checkbox"/> CU Cuba                                  | <input checked="" type="checkbox"/> PT Portugal                                  |
| <input checked="" type="checkbox"/> CZ Czech Republic                        | <input checked="" type="checkbox"/> RO Romania                                   |
| <input checked="" type="checkbox"/> DE Germany                               | <input checked="" type="checkbox"/> RU Russian Federation                        |
| <input checked="" type="checkbox"/> DK Denmark                               | <input checked="" type="checkbox"/> SD Sudan                                     |
| <input checked="" type="checkbox"/> EE Estonia                               | <input checked="" type="checkbox"/> SE Sweden                                    |
| <input checked="" type="checkbox"/> ES Spain                                 | <input checked="" type="checkbox"/> SG Singapore                                 |
| <input checked="" type="checkbox"/> FI Finland                               | <input checked="" type="checkbox"/> SI Slovenia                                  |
| <input checked="" type="checkbox"/> GB United Kingdom                        | <input checked="" type="checkbox"/> SK Slovakia                                  |
| <input checked="" type="checkbox"/> GE Georgia                               | <input checked="" type="checkbox"/> SL Sierra Leone                              |
| <input checked="" type="checkbox"/> GH Ghana                                 | <input checked="" type="checkbox"/> TJ Tajikistan                                |
| <input checked="" type="checkbox"/> GM Gambia                                | <input checked="" type="checkbox"/> TM Turkmenistan                              |
| <input checked="" type="checkbox"/> <del>GW Guinea-Bissau</del>              | <input checked="" type="checkbox"/> TR Turkey                                    |
| <input checked="" type="checkbox"/> HR Croatia                               | <input checked="" type="checkbox"/> TT Trinidad and Tobago                       |
| <input checked="" type="checkbox"/> HU Hungary                               | <input checked="" type="checkbox"/> UA Ukraine                                   |
| <input checked="" type="checkbox"/> ID Indonesia                             | <input checked="" type="checkbox"/> UG Uganda                                    |
| <input checked="" type="checkbox"/> IL Israel                                | <input checked="" type="checkbox"/> US United States of America                  |
| <input checked="" type="checkbox"/> IS Iceland                               |  |
| <input checked="" type="checkbox"/> JP Japan                                 |  |
| <input checked="" type="checkbox"/> KE Kenya                                 | <input checked="" type="checkbox"/> UZ Uzbekistan                                |
| <input checked="" type="checkbox"/> KG Kyrgyzstan                            | <input checked="" type="checkbox"/> VN Viet Nam                                  |
| <input checked="" type="checkbox"/> KP Democratic People's Republic of Korea | <input checked="" type="checkbox"/> YU Yugoslavia                                |
|  | <input checked="" type="checkbox"/> ZW Zimbabwe                                  |
| <input checked="" type="checkbox"/> KR Republic of Korea                     |  |
| <input checked="" type="checkbox"/> KZ Kazakhstan                            |  |
| <input checked="" type="checkbox"/> LC Saint Lucia                           |  |
| <input checked="" type="checkbox"/> LK Sri Lanka                             |  |
| <input checked="" type="checkbox"/> LR Liberia                               |  |

Check-boxes reserved for designating States (for the purposes of a national patent) which have become party to the PCT after issuance of this sheet:

- ☒ ~~HR Croatia~~
- ☒ GD Grenada

**Precautionary Designation Statement:** In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.)


<b>Box No. VI PRIORITY CLAIM</b>		<input type="checkbox"/> Further priority claims are indicated in the Supplemental Box.		
Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is:		
		national application: country	regional application:* regional Office	international application: receiving Office
item (1) 10 OCTOBER, 1997 (10.10.97)	PO9745	AUSTRALIA		
item (2)				
item (3)				

☐ The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) (only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office) identified above as item(s):

\* Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box.

<b>Box No. VII INTERNATIONAL SEARCHING AUTHORITY</b>		
<b>Choice of International Searching Authority (ISA)</b> (if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):  ISA /	<b>Request to use results of earlier search; reference to that search</b> (if an earlier search has been carried out by or requested from the International Searching Authority):  Date (day/month/year)      Number      Country (or regional Office)	

<b>Box No. VIII CHECK LIST; LANGUAGE OF FILING</b>	
This international application contains the following number of sheets:  request : 4 description (excluding sequence listing part) : 29 claims : 4 abstract : 1 drawings : 26 sequence listing part of description : 54 <b>Total number of sheets : 118</b>	This international application is <b>accompanied by</b> the item(s) marked below: 1. <input checked="" type="checkbox"/> fee calculation sheet 2. <input type="checkbox"/> separate signed power of attorney 3. <input type="checkbox"/> copy of general power of attorney; reference number, if any: 4. <input type="checkbox"/> statement explaining lack of signature 5. <input type="checkbox"/> priority document(s) identified in Box No. VI as item(s): 6. <input type="checkbox"/> translation of international application into (language): 7. <input type="checkbox"/> separate indications concerning deposited microorganism or other biological material 8. <input checked="" type="checkbox"/> nucleotide and/or amino acid sequence listing in computer readable form 9. <input checked="" type="checkbox"/> other (specify): <b>disquette (sequences)</b>
Figure of the drawings which should accompany the abstract:	Language of filing of the international application:

<b>Box No. IX SIGNATURE OF APPLICANT OR AGENT</b>	
Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).	
RHONE-POULENC AGRO   GENIN Patrick PG 1889	

For receiving Office use only		2. Drawings:  <input type="checkbox"/> received:  <input type="checkbox"/> not received:
1. Date of actual receipt of the purported international application:	<b>9 OCT. 1998</b> (09.10.1998)	
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:		
4. Date of timely receipt of the required corrections under PCT Article 11(2):		
5. International Searching Authority (if two or more are competent): ISA /		6. <input type="checkbox"/> Transmittal of search copy delayed until search fee is paid.

For International Bureau use only	
Date of receipt of the record copy by the International Bureau:	

## PCT COOPERATION TRE

PCT

NOTIFICATION CONCERNING  
SUBMISSION OR TRANSMITTAL  
OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

From the INTERNATIONAL BUREAU

To:

GENIN, Patrick  
Rhône-Poulenc Agro  
DPI  
14/20, rue Pierre Baize  
F-69009 Lyon  
FRANCE

REQU D.P.I.

- 1 FEVR 1999

Date of mailing (day/month/year) 22 February 1999 (22.02.99)	
Applicant's or agent's file reference PH 97069	IMPORTANT NOTIFICATION
International application No. PCT/EP98/06977	International filing date (day/month/year) 09 October 1998 (09.10.98)
International publication date (day/month/year) Not yet published	Priority date (day/month/year) 10 October 1997 (10.10.97)
Applicant RHONE-POULENC AGRO et al	

- The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).
- This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.
- An asterisk(\*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.
- The letters "NR" appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

<u>Priority date</u>	<u>Priority application No.</u>	<u>Country or regional Office or PCT receiving Office</u>	<u>Date of receipt of priority document</u>
10 Octo 1997 (10.10.97)	PO 9745	AU	12 Febr 1999 (12.02.99)

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer

Aino Metcalfe

Telephone No. (41-22) 338.83.38



TENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT



(PCT Article 36 and Rule 70)

REC'D 21 JAN 2000

WIPO PCT

Applicant's or agent's file reference PH 97069 PCT	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP98/06977	International filing date (day/month/year) 09/10/1998	Priority date (day/month/year) 10/10/1997
International Patent Classification (IPC) or national classification and IPC C12N15/29		
Applicant RHONE-POULENC AGRO et al.		

<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 8 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> <li>I <input checked="" type="checkbox"/> Basis of the report</li> <li>II <input checked="" type="checkbox"/> Priority</li> <li>III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</li> <li>IV <input type="checkbox"/> Lack of unity of invention</li> <li>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</li> <li>VI <input type="checkbox"/> Certain documents cited</li> <li>VII <input checked="" type="checkbox"/> Certain defects in the international application</li> <li>VIII <input checked="" type="checkbox"/> Certain observations on the international application</li> </ul>

Date of submission of the demand 03/05/1999	Date of completion of this report 17. 01. 00
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Burkhardt, P Telephone No. +49 89 2399 7456 

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP98/06977

**I. Basis of the report**

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

**Description, pages:**

1-29 as originally filed

**Claims, No.:**

1-35 as originally filed

**Drawings, sheets:**

1/28-28/28 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

**II. Priority**

1. ☐ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:
- ☐ copy of the earlier application whose priority has been claimed.
- ☐ translation of the earlier application whose priority has been claimed.
2. ☐ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid.

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP98/06977

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Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

**3. Additional observations, if necessary:**

**see separate sheet**

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Yes:	Claims	29, 30
	No:	Claims	1 - 28, 31 - 35
Inventive step (IS)	Yes:	Claims	29, 30
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1 - 35
	No:	Claims	

**2. Citations and explanations**

**see separate sheet**

**VII. Certain defects in the international application**

The following defects in the form or contents of the international application have been noted:

**see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/EP98/06977

**Re Item II**

**Priority**

As the priority document was not available at the time of drafting the present report, this report is being established under the assumption that the entire subject-matter is entitled to the claimed priority. If this is not the case, the 'P,X' documents cited in the search report may have to be considered for novelty and/or inventive step. These documents would be detrimental to some of the claimed subject-matter (Article 33(2), (3) PCT).

**Re Item V**

**Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

The following documents (D) are referred to in this communication; the numbering is following the order of the International Search Report:

D3 WO-A-9007576 (Setratech)

D6 Watanabe *et al.*, 1996. Genomics 31:311-318

The documents D16 and D17 were not cited in the international search report. Copies of the documents are appended hereto.

D16 Balestrazzi *et al.*, 1996. Gene 183:183-190

D17 WO-A-9626283 (Plant Genetic Systems)

**1. Article 33(2) PCT (Novelty)**

1.1 Present claim 1 addresses an "isolated and purified DNA molecule comprising a polynucleotide sequence encoding a polypeptide **functionally involved** in the DNA mismatch repair system of a plant".

Plant topoisomerases are involved in the modulation of conformational tension of chromatin to make the DNA accessible to housekeeping enzymes, like those of the mismatch repair system. Consequently, topoisomerases are functionally

involved in DNA mismatch repair. Topoisomerases are well characterised and are cloned from plants (e.g. D16). Therefore, the subject-matter of claim 1 is anticipated by said enzymes. The same holds true for dependent claim 2 and for claim 33.

1.2 The above applies *mutatis mutandis* to present claims 4 and 5 addressing purified proteins "functionally involved in the DNA mismatch repair system of a plant".

1.3 Present claim 3 addresses a DNA molecule encoding a polypeptide **homologous** to AtMSH3 (SEQ ID NO:19) or AtMSH6 (SEQ ID NO:31). According to the description (page 8, lines 13-16), polypeptides are homologous if they exhibit a similarity of at least 50% on the amino acid sequence level. D6 discloses the sequence of a human MSH3 gene. On the nucleic acid level it shares 59% identity in a 806 bp overlap with AtMSH3. The corresponding polypeptide appears to exhibit at least 50% similarity over certain stretches of its sequence. Therefore, the human MSH3 gene anticipates the subject-matter of claim 3. The same holds true for present claim 6 addressing polypeptides homologous to polypeptides encoded by AtMSH3 (SEQ ID NO:18) or AtMSH6 (SEQ ID NO:30). Present claims 3 and 6 do not meet the requirements of Article 33(2) PCT.

1.4 Oligonucleotides derived from the sequence of the human MSH3 gene disclosed in D6 appear to be capable of hybridising at 45°C under standard PCR conditions to SEQ ID NO:18 or NO:30. Therefore, present claims 34 and 35 do not meet the requirements of Article 33(2) PCT.

1.5 Present claim 7 addresses "an isolated and purified DNA molecule comprising (...) a sequence encoding a polynucleotide which is **capable of interfering with the expression of a plant polynucleotide** sequence encoding a polypeptide which is homologous to a mismatch repair polypeptide of a yeast or a human thereby disabling said plant polypeptide sequence".

The BARNase/BARstar® system is a well characterised system to eliminate and subsequently restore the activity of single cells (e.g. D17). The BARNase is an unspecific RNase that interferes with cellular RNAs, thereby blocking gene

expression in general. Consequently, the BARnase also interferes with the plant mismatch repair system. Therefore, D17 anticipates the subject-matter of present claim 7. The same holds true for dependent claims 8 - 12.

1.6 Present claim 13 addresses a chimeric gene comprising "a sequence encoding a polynucleotide which is **capable of interfering with the expression of a plant polynucleotide** sequence encoding a polypeptide which is homologous to a mismatch repair polypeptide of a yeast or a human thereby disabling said plant polypeptide sequence".

BARnase constructs (see 1.5) fall within the scope of claim 13 and therefore anticipate the subject-matter. The same holds true for dependent claims 14 - 17 as well as for present claims 18 - 23 addressing plants transformed with said constructs and processes for transforming plants with said constructs.

1.7 Present claim 24 addresses a process for increasing the genetic variation in a hybrid plant comprising altering the mismatch repair system in said plant.

Document D2 discloses a process for intergeneric recombination *in vivo* of partially homologous DNA sequences, these sequences being combined in cells or organisms of which the enzymatic mismatch repair system is defective or has been inactivated temporarily (page 30, claim 1). The cells for the *in vivo* cross are derived from organisms of different species and a least one of them is defective in the enzymatic mismatch repair system (page 31, claim 6). The organisms may be plants (page 31, claim 7).

In summary D2 discloses a method for increasing the genetic variation in plants comprising altering the mismatch repair system. Consequently, D2 anticipates the subject-matter of claim 24. The same holds true for claims 25/1 - 28, 31 and 32.

1.8 Present claims 29 and 30 further specify the process of claim 27 in that specific mismatch repair system genes are inactivated. Inactivation of these specific genes has not yet been disclosed in the prior art presently available to the IPEA. Claims 29 and 30 meet the requirements of Article 33(2) PCT.

## **2. Article 33(3) PCT (Inventive Step)**

2.1 The closest prior art for the remaining novel subject-matter is regarded as

being D2. The document discloses a method for increasing the genetic variation in plants comprising altering the mismatch repair system.

The subject-matter of novel claims 29 and 30 differs from that in the alteration of specific genes of the mismatch repair system. Altering these specific genes has not been suggested in the prior art presently available to the IPEA. Claims 29 and 30 meet the requirements of Article 33(3) PCT.

**Re Item VII**

**Certain defects in the international application**

The numbering of the claims should be checked for consistency as two claims 25 exist in the present set of claims.

**Re Item VIII**

**Certain observations on the international application**

1. The applicants have isolated and sequenced *Arabidopsis* genes which are homologous to mismatch repair (MMR) system genes in *E. coli*, yeast and humans. However, the analysis of the postulated function, i.e. involvement in the MMR system of *Arabidopsis*, is not provided. Consequently, claims relating to polypeptides functionally involved in the DNA MMR system, i.e. present claims 1 - 5 and 33, are not supported by the description (Article 6 PCT) as it appears to be impossible for a person skilled in the art to carry out the invention in order to arrive at the claimed subject-matter (Article 5 PCT).
2. Based on the cloning and sequencing of A $\mu$ MSH3 and A $\mu$ MSH6 it appears to be unjustified to extend the scope of the claims to structurally unrelated proteins equally involved in the mismatch repair system as the applicants did not contribute to the cloning of genes other than A $\mu$ MSH3 and A $\mu$ MSH6.
3. The term "functionally involved" used in present claim 1 is unclear (Article 6 PCT) It could be interpreted as embracing various cellular housekeeping proteins (see section V 1. above).

4. Claims 7 and 13 do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The following functional statements do not enable the skilled person to determine which technical features are necessary to perform the stated functions:

- (I) a polynucleotide **which is capable of interfering** with the expression of a plant polynucleotide sequence encoding a polypeptide which is homologous to a mismatch repair polypeptide ...
- (ii) a sequence encoding a polypeptide **capable of disrupting the DNA mismatch repair system of a plant.**

The same holds true for dependent claims 8 - 12 and 14 - 17 as well as for claims 18 - 20 and 21 - 23 addressing processes for **inactivating a plant MMR system** by transforming a plant cell with chimeric constructs as defined in claims 13 - 17 and transgenic plants transformed with said constructs.

5. Present independent claims 24 and 27 do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The following functional statements do not enable the skilled person to determine which technical features are necessary to perform the stated function:

- A process for **increasing genetic variation** in a plant comprising ... **altering the MMR system** in said (hybrid) plant ...
- A process for obtaining a plant having a desired characteristic , comprising **altering the MMR system** in a plant, ....

The same holds true for dependent claims 25/1 - 26 and 28 - 32.



PCT

**NOTICE INFORMING THE APPLICANT OF THE  
COMMUNICATION OF THE INTERNATIONAL  
APPLICATION TO THE DESIGNATED OFFICES**

(PCT Rule 47.1(c), first sentence)

From the INTERNATIONAL BUREAU

To:

GENIN, Patrick  
Rhône-Poulenc Agro  
DPI  
14/20, rue Pierre Baizet  
F-69009 Lyon  
FRANCE

REÇU D.P.I.

29 AVR. 1999

Date of mailing (day/month/year) 22 April 1999 (22.04.99)		IMPORTANT NOTICE	
Applicant's or agent's file reference PH 97069			
International application No. PCT/EP98/06977	International filing date (day/month/year) 09 October 1998 (09.10.98)	Priority date (day/month/year) 10 October 1997 (10.10.97)	
Applicant RHONE-POULENC AGRO et al			

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:  
AU,BR,CN,EP,IL,JP,KP,KR,US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:  
AL,AM,AP,AT,AZ,BA,BB,BG,BY,CA,CH,CU,CZ,DE,DK,EA,EE,ES,FI,GB,GD,GE,GH,GM,HR,HU,ID,IS,KE,KG,KZ,LC,LK,LR,LS,LT,LU,LV,MD,MG,MK,MN,MW,MX,NO,NZ,OA,PL,PT,RO,RU,SD,SE,SG,SI,SK,SL,TJ,TM,TR,TT,UA,UG,UZ,VN,YU,ZW  
The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).
3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on 22 April 1999 (22.04.99) under No. WO 99/19492

**REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)**

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a **demand for international preliminary examination** must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

**REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))**

If the applicant wishes to proceed with the international application in the **national phase**, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer  J. Zahra
Facsimile No. (41-22) 740.14.35	Telephone No. (41-22) 338.83.38

# PCT COOPERATION TREATY

# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>PH 97069</b>	<b>FOR FURTHER ACTION</b>		see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. <b>PCT/EP 98/ 06977</b>	International filing date (day/month/year) <b>09/10/1998</b>	(Earliest) Priority Date (day/month/year) <b>10/10/1997</b>	
Applicant  <b>RHONE-POULENC AGRO et al.</b>			

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☒ contained in the international application in written form.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 98/06977

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/82 C12N15/29 C07K14/415 C12N15/10 C12N5/04  
 C12N5/14 A01H5/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N A01H

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 95 15381 A (CHAPELLE ALBERT DE ;UNIV JOHNS HOPKINS (US)) 8 June 1995 see the whole document ---	1-5, 33-35
A	WO 97 37011 A (SETRATECH S A R L ;BORTS RHONA HARRIET (GB); LOUIS EDWARD JOHN (GB) 9 October 1997 see abstract see the whole document ---	1-35
A	WO 90 07576 A (SETRATECH) 12 July 1990  see the whole document and specially page 5, line 16-31, examples 3-4 --- -/--	1,7-27, 31,32



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

## \* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&amp;" document member of the same patent family

Date of the actual completion of the international search

16 April 1999

Date of mailing of the international search report

03/05/1999

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
 NL - 2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
 Fax: (+31-70) 340-3016

Authorized officer

Mateo Rosell, A.M.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/JP 98/06977

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 97 01634 A (ANGELETTI P IST RICHERCHE BIO ;JIRICNY JOSEF (IT); PALOMBO FABIO ()) 16 January 1997 see page 1, line 18 - page 2, line 28 see page 58 ---	1,2
A	PROLLA T A ET AL: "MLH1, PMS1, AND MSH2 INTERACTIONS DURING THE INITIATION OF DNA MISMATCH REPAIR IN YEAST" SCIENCE, vol. 265, 19 August 1994, pages 1091-1093, XP000676403 cited in the application ---	1,2,4,5
A	A. WATANABE ET AL., : "Genomic organization and expresssion of the human MSH3 gene" GENOMICS, vol. 31, 1996, pages 311-318, XP002099967 see the whole document and specially Fig.3 ---	1-6
A	ACHARYA S ET AL: "hMSH2 forms specific mispair-binding complexes with hMSH3 and hMSH6" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, no. 93, October 1996, pages 13629- 13629, XP002080159 cited in the application sequences from this paper deposited in GenBank under AC= U61981 (hMSH3), and U54777 and U73732-7 (hMSH6). see the whole document ---	1-6
A	K. LIU ET AL., : "characterization of the mouse Rep-3 gene: sequence similarities to bacterial and yeast mismatch-repair proteins" GENE, vol. 147, 1994, pages 169-177, XP002099968 see the whole document and specially Figure 2. ---	1-6
A	I. IACCARINO ET AL., : "MSH6, a Saccharomyces cerevisiae protein that binds to mismatches as a heterodimer with MSH2" CURRENT BIOLOGY, vol. 6, no. 4, April 1996, pages 484-486, XP002099969 sequence is deposited at GenBank under AC= Z47746. see the whole document ---	1-6

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## INTERNATIONAL SEARCH REPORT

International Application No.

PCT/EP 98/06977

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CORRADI A ET AL: "CDNA SEQUENCE, MAP, AND EXPRESSION OF THE MURINE HOMOLOG OF GTBP, ADNA MISMATCH REPAIR GENE" GENOMICS, vol. 36, no. 2, 1 September 1996, pages 288-295, XP000613761 see the whole document and specially Fig.1 ---	1-6
P,X	DATABASE EMBL NUCLEOTIDE AND PROTEIN SEQUENCES, 13 July 1998, XP002099368 HINXTON, GB AC= AJ007791. Arabidopsis thaliana mRNA for mismatch repair protein (MSH3) see abstract ---	1-6
P,X	DATABASE EMBL NUCLEOTIDE AND PROTEIN SEQUENCES, 1 August 1998, XP002099369 HINXTON, GB AC= 065607. Arabidopsis thaliana. Putative mismatch DNA repair protein see abstract ---	1-5
P,X	DATABASE EMBL NUCLEOTIDE AND PROTEIN SEQUENCES, 16 October 1997, XP002099371 HINXTON, GB AC= AF009657. Arabidopsis thalian Muts homolog 6-like protein mRNA. see abstract -& K.M. CULLIGAN AND J.B. HAYS: "DNA mismatch repair in plants" PLANT PHYSIOLOGY, vol. 115, 1997, pages 833-839, XP002099372 see the whole document ---	1-6
T	DATABASE EMBL NUCLEOTIDE AND PROTEIN SEQUENCES, 17 December 1998, XP002099373 HINXTON, GB AC= AJ131669. Triticum aestivum mRNA for MSH3 protein, MSH3 gene. see abstract ---	1-6
T	DATABASE EMBL NUCLEOTIDE AND PROTEIN SEQUENCES, 12 October 1998, XP002099370 HINXTON, GB AC= AJ007792. Arabidopsis thaliana DNA mismatch repair protein, MSH6 gene. see abstract -----	1-6

# INTERNATIONAL SEARCH REPORT

Info on patent family members

International Application No

PCT/EP 98/06977

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9515381	A	08-06-1995	EP 0730648 A	11-09-1996
			JP 9506509 T	30-06-1997
			US 5693470 A	02-12-1997
			US 5837443 A	17-11-1998
WO 9737011	A	09-10-1997	NONE	
WO 9007576	A	12-07-1990	FR 2641793 A	20-07-1990
			AT 127519 T	15-09-1995
			AU 4834390 A	01-08-1990
			CA 2006549 A	26-06-1990
			DE 68924174 D	12-10-1995
			DE 68924174 T	14-03-1996
			EP 0449923 A	09-10-1991
			ES 2077058 T	16-11-1995
			IE 72469 B	09-04-1997
			JP 4503601 T	02-07-1992
WO 9701634	A	16-01-1997	IT RM950434 A	27-12-1996
			AU 6241296 A	30-01-1997

# PATENT COOPERATION TREATY

J  
J

REÇU D.P.I

24 JAN. 2000

PCT

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

TETAZ, Franck  
RHONE-POULENC AGRO  
14/20 Rue Pierre Baizet  
F-69009 Lyon  
FRANCE

U<sup>v</sup>

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT  
(PCT Rule 71.1)

Date of mailing  
(day/month/year)

17. 01. 00

Applicant's or agent's file reference  
**PH 97069 PCT**

## IMPORTANT NOTIFICATION

International application No.  
PCT/EP98/06977

International filing date (day/month/year)  
09/10/1998

Priority date (day/month/year)  
10/10/1997

Applicant  
RHONE-POULENC AGRO et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

#### 4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/

 European Patent Office  
D-80298 Munich  
Tel. +49 89 2399 - 0 Tx: 523656 epmu d  
Fax: +49 89 2399 - 4465

Authorized officer

Vullo, C

Tel.+49 89 2399-8061



# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>PH 97069 PCT</b>	<div style="display: flex; justify-content: space-between;"> <div><b>FOR FURTHER ACTION</b></div> <div>See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)</div> </div>	
International application No. <b>PCT/EP98/06977</b>	International filing date (day/month/year) <b>09/10/1998</b>	Priority date (day/month/year) <b>10/10/1997</b>
International Patent Classification (IPC) or national classification and IPC <b>C12N15/29</b>		
Applicant <b>RHONE-POULENC AGRO et al.</b>		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 8 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☒ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand  <b>03/05/1999</b>	Date of completion of this report  <b>17. 01. 00</b>
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer  <b>Burkhardt, P</b>  Telephone No. +49 89 2399 7456 



# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP98/06977

## 1. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

### Description, pages:

1-29 as originally filed

### Claims, No.:

1-35 as originally filed

### Drawings, sheets:

1/28-28/28 as originally filed

## 2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

## 4. Additional observations, if necessary:

## II. Priority

1. ☐ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:
- ☐ copy of the earlier application whose priority has been claimed.
  - ☐ translation of the earlier application whose priority has been claimed.
2. ☐ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid.

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP98/06977

Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

**see separate sheet**

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes:	Claims	29, 30
	No:	Claims	1 - 28, 31 - 35
Inventive step (IS)	Yes:	Claims	29, 30
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1 - 35
	No:	Claims	

2. Citations and explanations

**see separate sheet**

**VII. Certain defects in the international application**

The following defects in the form or contents of the international application have been noted:

**see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/EP98/06977

**Re Item II**

**Priority**

As the priority document was not available at the time of drafting the present report, this report is being established under the assumption that the entire subject-matter is entitled to the claimed priority. If this is not the case, the 'P,X' documents cited in the search report may have to be considered for novelty and/or inventive step. These documents would be detrimental to some of the claimed subject-matter (Article 33(2), (3) PCT).

**Re Item V**

**Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

The following documents (D) are referred to in this communication; the numbering is following the order of the International Search Report:

D3 WO-A-9007576 (Setratech)

D6 Watanabe *et al.*, 1996. Genomics 31:311-318

The documents D16 and D17 were not cited in the international search report. Copies of the documents are appended hereto.

D16 Balestrazzi *et al.*, 1996. Gene 183:183-190

D17 WO-A-9626283 (Plant Genetic Systems)

**1. Article 33(2) PCT (Novelty)**

1.1 Present claim 1 addresses an "isolated and purified DNA molecule comprising a polynucleotide sequence encoding a polypeptide **functionally involved** in the DNA mismatch repair system of a plant".

Plant topoisomerases are involved in the modulation of conformational tension of chromatin to make the DNA accessible to housekeeping enzymes, like those of the mismatch repair system. Consequently, topoisomerases are functionally

involved in DNA mismatch repair. Topoisomerases are well characterised and are cloned from plants (e.g. D16). Therefore, the subject-matter of claim 1 is anticipated by said enzymes. The same holds true for dependent claim 2 and for claim 33.

1.2 The above applies *mutatis mutandis* to present claims 4 and 5 addressing purified proteins "functionally involved in the DNA mismatch repair system of a plant".

1.3 Present claim 3 addresses a DNA molecule encoding a polypeptide **homologous** to AtMSH3 (SEQ ID NO:19) or AtMSH6 (SEQ ID NO:31). According to the description (page 8, lines 13-16), polypeptides are homologous if they exhibit a similarity of at least 50% on the amino acid sequence level. D6 discloses the sequence of a human MSH3 gene. On the nucleic acid level it shares 59% identity in a 806 bp overlap with AtMSH3. The corresponding polypeptide appears to exhibit at least 50% similarity over certain stretches of its sequence. Therefore, the human MSH3 gene anticipates the subject-matter of claim 3. The same holds true for present claim 6 addressing polypeptides homologous to polypeptides encoded by AtMSH3 (SEQ ID NO:18) or AtMSH6 (SEQ ID NO:30). Present claims 3 and 6 do not meet the requirements of Article 33(2) PCT.

1.4 Oligonucleotides derived from the sequence of the human MSH3 gene disclosed in D6 appear to be capable of hybridising at 45°C under standard PCR conditions to SEQ ID NO:18 or NO:30. Therefore, present claims 34 and 35 do not meet the requirements of Article 33(2) PCT.

1.5 Present claim 7 addresses "an isolated and purified DNA molecule comprising (...) a sequence encoding a polynucleotide which is **capable of interfering with the expression of a plant polynucleotide** sequence encoding a polypeptide which is homologous to a mismatch repair polypeptide of a yeast or a human thereby disabling said plant polypeptide sequence".

The BARnase/BARstar® system is a well characterised system to eliminate and subsequently restore the activity of single cells (e.g. D17). The BARnase is an unspecific RNase that interferes with cellular RNAs, thereby blocking gene

expression in general. Consequently, the BARnase also interferes with the plant mismatch repair system. Therefore, D17 anticipates the subject-matter of present claim 7. The same holds true for dependent claims 8 - 12.

1.6 Present claim 13 addresses a chimeric gene comprising "a sequence encoding a polynucleotide which is **capable of interfering with the expression of a plant polynucleotide** sequence encoding a polypeptide which is homologous to a mismatch repair polypeptide of a yeast or a human thereby disabling said plant polypeptide sequence".

BARnase constructs (see 1.5) fall within the scope of claim 13 and therefore anticipate the subject-matter. The same holds true for dependent claims 14 - 17 as well as for present claims 18 - 23 addressing plants transformed with said constructs and processes for transforming plants with said constructs.

1.7 Present claim 24 addresses a process for increasing the genetic variation in a hybrid plant comprising altering the mismatch repair system in said plant. Document D2 discloses a process for intergeneric recombination *in vivo* of partially homologous DNA sequences, these sequences being combined in cells or organisms of which the enzymatic mismatch repair system is defective or has been inactivated temporarily (page 30, claim 1). The cells for the *in vivo* cross are derived from organisms of different species and a least one of them is defective in the enzymatic mismatch repair system (page 31, claim 6). The organisms may be plants (page 31, claim 7).

In summary D2 discloses a method for increasing the genetic variation in plants comprising altering the mismatch repair system. Consequently, D2 anticipates the subject-matter of claim 24. The same holds true for claims 25/1 - 28, 31 and 32.

1.8 Present claims 29 and 30 further specify the process of claim 27 in that specific mismatch repair system genes are inactivated. Inactivation of these specific genes has not yet been disclosed in the prior art presently available to the IPEA. Claims 29 and 30 meet the requirements of Article 33(2) PCT.

## **2. Article 33(3) PCT (Inventive Step)**

2.1 The closest prior art for the remaining novel subject-matter is regarded as

being D2. The document discloses a method for increasing the genetic variation in plants comprising altering the mismatch repair system.

The subject-matter of novel claims 29 and 30 differs from that in the alteration of specific genes of the mismatch repair system. Altering these specific genes has not been suggested in the prior art presently available to the IPEA. Claims 29 and 30 meet the requirements of Article 33(3) PCT.

**Re Item VIII**

**Certain defects in the international application**

The numbering of the claims should be checked for consistency as two claims 25 exist in the present set of claims.

**Re Item VIII**

**Certain observations on the international application**

1. The applicants have isolated and sequenced *Arabidopsis* genes which are homologous to mismatch repair (MMR) system genes in *E. coli*, yeast and humans. However, the analysis of the postulated function, i.e. involvement in the MMR system of *Arabidopsis*, is not provided. Consequently, claims relating to polypeptides functionally involved in the DNA MMR system, i.e. present claims 1 - 5 and 33, are not supported by the description (Article 6 PCT) as it appears to be impossible for a person skilled in the art to carry out the invention in order to arrive at the claimed subject-matter (Article 5 PCT).
2. Based on the cloning and sequencing of A#MSH3 and A#MSH6 it appears to be unjustified to extend the scope of the claims to structurally unrelated proteins equally involved in the mismatch repair system as the applicants did not contribute to the cloning of genes other than A#MSH3 and A#MSH6.
3. The term "functionally involved" used in present claim 1 is unclear (Article 6 PCT) It could be interpreted as embracing various cellular housekeeping proteins (see section V 1. above).

4. Claims 7 and 13 do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The following functional statements do not enable the skilled person to determine which technical features are necessary to perform the stated functions:

- (i) a polynucleotide **which is capable of interfering** with the expression of a plant polynucleotide sequence encoding a polypeptide which is homologous to a mismatch repair polypeptide ...
- (ii) a sequence encoding a polypeptide **capable of disrupting the DNA mismatch repair system of a plant.**

The same holds true for dependent claims 8 - 12 and 14 - 17 as well as for claims 18 - 20 and 21 - 23 addressing processes for **inactivating a plant MMR system** by transforming a plant cell with chimeric constructs as defined in claims 13 - 17 and transgenic plants transformed with said constructs.

5. Present independent claims 24 and 27 do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The following functional statements do not enable the skilled person to determine which technical features are necessary to perform the stated function:

- A process for **increasing genetic variation** in a plant comprising ... **altering the MMR system** in said (hybrid) plant ...
- A process for obtaining a plant having a desired characteristic , comprising **altering the MMR system** in a plant, ....

The same holds true for dependent claims 25/1 - 26 and 28 - 32.

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PH 97069 PCT	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP98/06977	International filing date (day/month/year) 09/10/1998	Priority date (day/month/year) 10/10/1997
International Patent Classification (IPC) or national classification and IPC C12N15/29		
Applicant RHONE-POULENC AGRO et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 8 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☒ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand  03/05/1999	Date of completion of this report  7. 01. 00
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer  Burkhardt, P  Telephone No. +49 89 2399 7456 



# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP98/06977

## I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

### Description, pages:

1-29 as originally filed

### Claims, No.:

1-35 as originally filed

### Drawings, sheets:

1/28-28/28 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

## II. Priority

1. ☐ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:
- ☐ copy of the earlier application whose priority has been claimed.
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# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP98/06977

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3. Additional observations, if necessary:

**see separate sheet**

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Novelty (N)	Yes:	Claims	29, 30
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Inventive step (IS)	Yes:	Claims	29, 30
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1 - 35
	No:	Claims	

2. Citations and explanations

**see separate sheet**

## VII. Certain defects in the international application

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**Re Item II**

**Priority**

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**1. Article 33(2) PCT (Novelty)**

1.1 Present claim 1 addresses an "isolated and purified DNA molecule comprising a polynucleotide sequence encoding a polypeptide **functionally involved** in the DNA mismatch repair system of a plant".

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1.7 Present claim 24 addresses a process for increasing the genetic variation in a hybrid plant comprising altering the mismatch repair system in said plant. Document D2 discloses a process for intergeneric recombination *in vivo* of partially homologous DNA sequences, these sequences being combined in cells or organisms of which the enzymatic mismatch repair system is defective or has been inactivated temporarily (page 30, claim 1). The cells for the *in vivo* cross are derived from organisms of different species and a least one of them is defective in the enzymatic mismatch repair system (page 31, claim 6). The organisms may be plants (page 31, claim 7).

In summary D2 discloses a method for increasing the genetic variation in plants comprising altering the mismatch repair system. Consequently, D2 anticipates the subject-matter of claim 24. The same holds true for claims 25/1 - 28, 31 and 32.

1.8 Present claims 29 and 30 further specify the process of claim 27 in that specific mismatch repair system genes are inactivated. Inactivation of these specific genes has not yet been disclosed in the prior art presently available to the IPEA. Claims 29 and 30 meet the requirements of Article 33(2) PCT.

## **2. Article 33(3) PCT (Inventive Step)**

2.1 The closest prior art for the remaining novel subject-matter is regarded as

being D2. The document discloses a method for increasing the genetic variation in plants comprising altering the mismatch repair system.

The subject-matter of novel claims 29 and 30 differs from that in the alteration of specific genes of the mismatch repair system. Altering these specific genes has not been suggested in the prior art presently available to the IPEA. Claims 29 and 30 meet the requirements of Article 33(3) PCT.

**Re Item VIII**

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4. Claims 7 and 13 do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The following functional statements do not enable the skilled person to determine which technical features are necessary to perform the stated functions:

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5. Present independent claims 24 and 27 do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The following functional statements do not enable the skilled person to determine which technical features are necessary to perform the stated function:

- A process for **increasing genetic variation** in a plant comprising ... **altering the MMR system** in said (hybrid) plant ...
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The same holds true for dependent claims 25/1 - 26 and 28 - 32.